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(54) Title: USE OF AN EXTRACT OF DECAFFEINATED COFFEE BEANS IN THE PREPARATION OF A COMPOSITION INTENDED TO CORRECT OR PREVENT THE DISORDERS ASSOCIATED WITH A GREASY SKIN BY TOPICAL ADMINISTRATION

(57) Abstract: The present invention relates to the use of an extract of decaffeinated coffee grains in the preparation of a composition intended to correct or prevent the disorders associated with a greasy skin in particular by an action diminishing the secretion of the sebum by topical administration. The invention relates in particular to cosmetic compositions intended for administration by the topical route. The invention also relates to a cosmetic procedure for correcting or preventing the disorders associated with a hyperseborrhea.

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**USE OF AN EXTRACT OF DECAFFEINATED COFFEE BEANS
IN THE PREPARATION OF A COMPOSITION INTENDED
TO CORRECT OR PREVENT THE DISORDERS ASSOCIATED
WITH A GREASY SKIN BY TOPICAL ADMINISTRATION**

5 The present invention relates to the use of an extract of decaffeinated coffee grains in the preparation of a composition intended to correct or prevent the disorders associated with a greasy skin in particular by an action diminishing the secretion of the sebum by topical administration. The invention relates in particular to cosmetic compositions intended for
10 administration by the topical route. The invention also relates to a cosmetic procedure for correcting or preventing the disorders associated with a hyperseborrhea.

A hyperseborrheic greasy skin is characterised by an excessive secretion and excretion of sebum. Conventionally, a concentration of sebum higher
15 than 200 $\mu\text{g}/\text{cm}^2$ measured on the forehead is considered as characteristic of such a greasy skin.

A greasy skin is often associated with a desquamation deficiency, a glossy complexion, a coarse-textured skin.

In addition to these aesthetic disorders, the excess of sebum can serve to
20 support the sporadic development of the saprophytic bacterial flora (p. acnes in particular) and cause comedones and/or acneic lesions.

The sebum is the natural product of the sebaceous gland which constitutes an adnex of the pilosebaceous unit. It is essentially a quite complex mixture of lipids. Usually, the sebaceous gland produces squalene, triglycerides,
25 aliphatic waxes, cholesterol waxes and, possibly, free cholesterol (Stewart, M.E., Semin. Dermatol 11, 100-105 (1992). The action of bacterial lipases converts a variable part of the triglycerides formed into free fatty acids.

The sebocyte constitutes the competent cell of the sebaceous gland. The production of sebum is associated with a programme of terminal differentiation of this cell. During this differentiation, the metabolic activity of the sebocyte is essentially directed to the biosynthesis of lipids (lipogenesis) and more particularly to the de novo synthesis of fatty acids.

The invention results from the demonstration of the fact that the topical administration of a composition containing an extract of decaffeinated coffee beans can diminish lipogenesis at the level of the sebocytes and consequently limit the production of sebum.

Coffee trees are small trees with smooth-margined, perennial, coriaceous, glossy leaves (10-15 x 4-6 cm). The white, fragrant flowers are grouped in whorls at the axil of the leaves. The fruit is a green drupe, which becomes red at maturity and usually contains two planar-convex berries which are made contiguous through their planar face. Although only two species supply the essential needs of the coffee market (*C. arabica* and *C. canephora*), many species of coffee trees exist in the wild state in the tropical forests of East Africa.

The berry is oval (10-15 x 6-8 mm), convex on the dorsal face, flattened on the ventral face which is traversed by a longitudinal groove, the hilum. Hard and greenish, it is odourless. The microscopic examination of the green coffee powder reveals fusiform fibres derived from the tegument and cells of albumen: polyhedral, their wall is nacreous and irregularly thickened in a bead-like structure; they contain oily droplets.

The coffee "bean" is obtained by the moist route (fermentation, washing) or the dry route (drying, followed by mechanical decortication) starting from the coffee "cherry", i.e. from the drupes. The reduction to pulp removes the red epicarp and the fleshy mesocarp; it leads to the coffee "husk". It is after husking (removal of the lignified endocarp) that the coffee "berry" (or bean) is obtained.

More than 50% of the dry matter of the green coffee berry are represented by carbohydrates, essentially polysaccharides. The proteins represent 10 to 12% of this mass, the lipids 10 to 18%. The unsaponifiable fraction of the crude lipids is considerable (more than 10%): in addition to sterols, hydrocarbons, tocopherols, diterpenic alcohols (cafestol, kahweol and kauranic derivatives) are observed to be present in the free state and, in particular, in the state of fatty acid esters. The coffee berry contains about 5% of phenolic acids: quinic acid, caffeic acid, chlorogenic acid. The caffeine content is variable: from 0.6 to 2% and more than 3% for certain canephora (robusta variety).

On torrefaction the texture and the composition of the berry change considerably. The water content is reduced, the berry swells, the polysaccharides are very degraded (forming in particular soluble products), pigments form (polycondensed furans) and the extremely complex flavour develops (several hundred compounds: alcohols, phenols, aldehydes, furanic and pyrrolic derivatives, hydrocarbons, thiophenes, etc.).

As far as the applicant is aware, it has never been suggested that an extract of decaffeinated coffee beans be used in the preparation of a composition formulated for oral administration and intended for the stimulation of the sebaceous function of the skin, in particular for the treatment of greasy skins.

Hence the object of the invention is the use of an extract of decaffeinated coffee beans in the preparation of a topical composition intended to moderate the sebaceous function of the skin.

In the text which follows "coffee beans" must be understood to mean the bean obtained by the moist route (fermentation, washing) or by the dry route (drying followed by mechanical husking) starting from the coffee "cherry", after husking as described above.

"Extract" must be understood to mean all of the compounds obtained starting from an alcoholic or aqueous-alcoholic extraction of a crude product, in this instance decaffeinated coffee beans, roasted or unroasted.

5 The production of sebum by the skin can be determined by the measurement of the amount of sebum according to the standard so-called sebumetric procedure described, for example, in the L'Oréal patent FR 2368708 or FR 2404845.

By "stimulation of the sebaceous function of the skin" is meant a significant stimulation of the amount of sebum in the skin.

10 The species of coffee trees selected for the preparation of the extracts of coffee beans used in the compositions are advantageously selected from the *Coffea* species.

In a particular embodiment, the extract is derived from coffee beans selected from the species *Coffea arabica*, *Coffea canephora* or *Coffea*
15 *iberica*. The extract may be obtained starting from roasted coffee beans. It can also be obtained from unroasted coffee beans.

For use according to the invention, the extract of coffee beans is decaffeinated.

20 In particular, a coffee bean extract can be obtained by an aqueous-alcoholic or alcoholic extraction of coffee beans, and preferably by an extraction with the aid of methanol, ethanol or propanol. Preferably, it does not contain the fractions of coffee beans extractable by non-polar solvents.

The invention also relates to cosmetic compositions containing the extract of decaffeinated coffee beans, intended to moderate the sebaceous
25 function of the skin by the topical route. In particular, the compositions according to the invention are intended for the treatment and/or the prevention of greasy skins. The proportion of decaffeinated coffee bean

extract in the composition will of course be determined as a function of the desired effect on the moderation of the sebaceous function of the skin and the mode of administration of the composition.

Since the composition containing an extract of decaffeinated coffee beans
5 is formulated for topical administration, the coffee bean extract is present in the composition in a quantity ranging from 0.0001 to 20% by weight, and preferably from 0.001 to 10%.

Chlorogenic acid which is a phenolic compound naturally present in some coffee bean extracts is not involved in the treatment of dry skins.
10 Chlorogenic acid is thus not an active agent of the compositions for the treatment and/or the prevention of dry skins according to the invention.

Preferably, chlorogenic acid is present in the composition according to the invention in an amount inferior or equal to 0,1% by weight of chlorogenic acid.

15 A composition formulated for topical administration according to the invention contains a cosmetically or dermatologically acceptable medium, a medium compatible with administration to or contact with the skin, nails, mucous membranes, the tissues and the hair. According to a preferred embodiment of the invention, the composition has a preferred pH close to
20 that of the skin, included between 4 and 7. The composition containing an extract of decaffeinated coffee beans is preferably applied topically to the face, neck, hair, mucous membranes and nails or any other exposed part of the body. It is most preferably applied to the greasy parts of the face.

A cosmetic composition according to the invention may be available in all of
25 the galenic forms usually used in the cosmetic and dermatological fields. In particular it may be available in the form of aqueous-alcoholic or oily solutions, dispersions of the lotion or serum type, anhydrous or oily gels, emulsions of liquid or semi-liquid consistency of the milk type, obtained by

dispersion of a fatty phase in an aqueous phase (O/W) or the inverse (W/O), or a triple emulsion (W/O/W or O/W/O), suspensions or emulsions of soft, semi-solid or solid consistency of the cream and gel type, micro-emulsions or also micro-capsules, micro-particles or vesicular dispersions
5 of the ionic and/or non-ionic type. These compositions are prepared according to the usual methods.

The quantities of the different constituents of the compositions used according to the invention are those conventionally used in the fields considered.

10 These compositions constitute in particular creams for the protection, treatment or care of the face, the hands or body, care or protection body milks, lotions, gels or foams for the care of the skin and mucous membranes or for cleansing the skin.

The compositions may also consist of solid preparations consisting of
15 soaps or blocks of soap.

It is known that the composition used according to the invention may also contain adjuvants usually used in the cosmetic and dermatological fields, such as hydrophilic or lipophilic gelling agents, hydrophilic or lipophilic active agents, preservatives, antioxidants, solvents, perfumes, fillers and
20 colouring matters. The quantities of these different adjuvants are those used conventionally in the fields considered, for example from 0.01% to 20% of the total weight of the composition. Naturally, the specialist will take care to select that or those possible additives and/or their quantities such that the advantageous properties intrinsically attached to the composition
25 conform to the invention.

As oils which can be used in the invention, mention may be made of the mineral oils (vaseline oil), the vegetable oils (shea butter oil, sweet almond oil), the animal oils, synthetic oils, siliconized oils (cyclomethicone) and the

fluorinated oils (perfluoropolyethers). Use may also be made as fatty materials of fatty alcohols, fatty acids (stearic acid) and waxes (paraffin, carnauba, beeswax).

As emulsifiers which can be used in the invention, mention may be made of polysorbate 60 and sorbitan stearate marketed respectively under the trade names Tween 60 and Span 60 by the ICI Company. Co-emulsifiers such as PPG-3 myristyl ether sold under the trade name Emcol 249-3K by the Witco Company may also be added.

Mention may be made of the lower alcohols, in particular ethanol, isopropanol and propylene glycol as solvents which can be used in the invention.

As hydrophilic gelling agents, mention may be made of the carboxyvinyl polymers (carbomer), the acrylic copolymers such as the acrylates/alkylacrylate copolymers, the polyacrylamides, the polysaccharides such as hydroxypropylcellulose, natural gums (xanthan) and the clays and, as lipophilic gelling agents mention may be made of the modified clays like the bentones, the metallic sols of fatty acids like the aluminium stearates, hydrophobic silica, the polyethylenes and ethylcellulose.

As hydrophilic active compounds, use may be made of the proteins or protein hydrolysates, the amino acids, the polyols, urea, allantoin, the sugars and sugar derivatives, water-soluble vitamins, starch, bacterial or plant extracts, in particular Aloe Vera.

As lipophilic active compounds, use may be made of tocopherol (vitamin E) and its derivatives, the essential fatty acids, the ceramides, the essential oils.

For the purpose of effective control of photo-ageing it is also possible to add to the composition used according to the invention one or more complementary solar filters, active in the UVA and/or UVB, hydrophilic or lipophilic, and possibly comprising a sulfonic function.

- 5 The solar filter is preferably selected from the organic and/or mineral filters.

As organic filters, particular mention may be made of the cinnamic derivatives, the salicylic derivatives, the camphor derivatives, the triazine derivatives, the benzophenone derivatives, the dibenzoylmethane derivatives, the β,β -diphenyl acrylate derivatives, the p-aminobenzoic acid
10 derivatives, the polymer filters and the silicone filters described in the application WO-93/4665 or also the organic filters described in the patent application EP-A 0 487 404.

As mineral filters, particular mention may be made of the pigments or even of the nanopigments (mean size of primary particles: usually between 5 nm
15 and 10 nm, and preferably between 10 and 50 nm) of coated or uncoated metal oxides like, for example, nanopigments of the oxides of titanium (amorphous or crystalline in the form of rutile and/or octahedrite), iron, zinc, zirconium or cerium which are all photoprotective agents well-known to act
20 as physical blockers of UV radiation. Conventional coating agents are moreover alumina and/or aluminium stearate. Such metal oxide nanopigments, coated or uncoated, are described in particular in the patent applications EP-A-0 518 772 and EP-A-0 518 773.

As examples of complementary solar filters active in the UV-A and/or the UV-B, mention may be made of:

- 25 p-aminobenzoic acid,
oxyethylenated p-aminobenzoate (25 mol),
2-ethylhexyl p-dimethylaminobenzoate,
N-oxypropylenated ethyl p-aminobenzoate,

- glyceryl p-aminobenzoate,
homomenthyl salicylate,
2-ethylhexyl salicylate,
triethanolamine salicylate,
5 4-isopropylbenzyl salicylate,
4-tert.butyl-4'-methoxy-dibenzoylmethane (PARSOL 1789 from GIVAUDAN
ROURE)
2-ethylhexyl p-methoxycinnamate (PARSOL MCX from GIVAUDAN
ROURE)
10 4-isopropyl-dibenzoylmethane(EUSOLEX 8020 from MERCK)
menthyl anthranilate,
2-ethylhexyl-2-cyano-3,3'-diphenylacrylate(UVINUL N539 from BASF)
ethyl-2-cyano-3,3'-diphenylacrylate,
2-phenyl benzimidazole 5-sulfonic acid and its salts,
15 3-(4'-trimethylammonium)-benzylidene-bornan-2-one methylsulfate,
2-hydroxy-4-methoxybenzophenone (UVINUL MS 40 from BASF),
2-hydroxy-4-methoxybenzophenone-5-sulfonate (UVINUL MS 40 from
BASF),
2,4-dihydroxybenzophenone (UVINUL 400 from BASF),
20 2,2',4,4'-tetrahydroxybenzophenone (UVINUL D 50 from BASF)
2,2'-dihydroxy-4,4'-dimethoxybenzophenone (HELISORB II from
NORQUAY),
2-hydroxy-4-n-octoxybenzophenone,
2-hydroxy-4-methoxy-4'-methylbenzophenone,
25 α -(2-oxoborn-3-ylidene)-tolyl-4-sulfonic acid and its alts,
3-(4'-sulfo) benzylidene-bornan-2-one and its salts,
3-(4'-methylbenzylidene)-d,l-camphor,
3-benzylidene-d,l-camphor,
benzene 1,4-di (3-methylidene-10-camphosulfonic) acid and its salts
30 (MEXORYL SX from CHIMEX),
urocanic acid,

2,4,6-tris [p-(2'-ethylhexyl-1'-oxycarbonyl)anilino]-1,3,5-triazine,
 2- [p-(tert.butylamido)anilino]-4,6-bis [p-(24-ethylhexyl-1'-
 oxycarbonyl)anilino]-1,3,5-triazine,
 2,4-bis {[4-2-ethyl-hexyloxy]-2-hydroxyl-phenyl}-6-(4-methoxy-phenyl)-
 5 1,3,5-triazine,
 the polymer of N-(2 and 4)-[2-oxoborn-3-ylidene) methyl) benzyl]-
 acrylamide,
 4,4-bis-benzimidazolyl-phenylene-3,3',5,5'-tetrasulfonic acid and its salts,
 2,2'-methylene-bis-[6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)
 10 phenol],
 the polyorganosiloxanes with malonate function.

The invention also relates to a cosmetic treatment procedure by the
 application of the compositions such as defined above according to the
 usual procedure of use of these compositions. For example: application of
 15 creams, gels, serums, ointments, lotions, milks to the skin, scalp, nails
 and/or mucous membranes.

The invention relates in particular to a cosmetic procedure for the treatment
 and/or prevention of greasy skins which consists of applying to the skin, the
 mucous membranes and/or keratinic fibres a composition containing a
 20 decaffeinated coffee bean extract.

In one particular embodiment, the cosmetic procedure comprises the steps
 of applying to the greasy parts of the face a composition containing a
 decaffeinated coffee bean extract, once or twice a day.

The characteristics of the invention mentioned above as well as others will
 25 become more clearly apparent in the light of the Examples presented
 hereafter.

EXAMPLES

Example 1: Preparation of a roasted extract of *Coffea robusta*

0.5 kg of roasted coffee beans is reduced to a powder by grinding with the Turrax apparatus at 24000 rev/min for 1 minute at 4°C (ice bath).

- 5 The powder obtained is mixed with 5 litres of 0.05M phosphate buffer at pH 8.5. The entire mixture is stirred for 30 minutes at 4°C, then centrifuged at 10 000 G at 4°C. The supernatant is filtered through a 0.22 µm filter (sterilizing filtration).

10 The extract is then fractionated by ultrafiltration through a Sartorius type membrane in order to remove from it oxidation phenomena.

The extract is then lyophilized. 29.5 grams of active extract called "lyophilized extract" are thus obtained.

15 Caffeine is then removed by supercritical chromatography (CO₂ is used as carrier gas). 25.5 grams of active extract called "decaffeinated lyophilized extract" are thus obtained.

Example 2: Demonstration of the sebomoderating activity of a decaffeinated coffee bean extract in comparison with a non-decaffeinated coffee bean extract.

20 Two lyophilized coffee extracts, decaffeinated (EXTRACT 1) and non-decaffeinated (EXTRACT 2) were tested on a model of human sebocytes immortalized in culture, derived from the line SZ95 described in Zouboulis, C.C., Seltmann, H., Neitzel, H. & Orfanos, C.E., Establishment and Characterization of an Immortalized Human Sebaceous Gland Cell Line, J. Invest. Dermatol., 113, 1011-1020 (1999). These extracts were prepared

according to Example 1, the last step being omitted in the case of EXTRACT 2.

The test consisted of measuring the quantity of lipids produced by the sebocytes of the line (to confluence), in the presence or absence of active agents diluted in the culture medium. After 2 days of treatment, the adherent cells are treated by Nile Red (1 $\mu\text{g/ml}$). The lipid content is then quantified by measurement of the fluorescence of the dye (two excitation/emission couples: 485-540 nm for the neutral lipids and 540-620 nm for the non-neutral lipids). The results are given for the neutral lipids (sebum constituents) (1st line of the table).

The experiment is performed in octuplicate (analyzed products and control) in 96 well plates.

The results are presented in the table below:

	C	EXTRACT 2			EXTRACT 1		
		4.10-5%	4.10-4%	4.10-3%	4.10-5%	4.10-4%	4.10-3%
Mean	8425	9123	8001	9150	8090	8705	6182
Std.dev.	1028	827	685	1160	1370	914	655
% of C	Ref.	108	95	109	96	103	73
Student	Ref.	0.14586	0.31577	0.22668	0.61147	0.56835	0.00004

EXTRACT 1 (decaffeinated) inhibits the production of neutral lipids significantly at 4.10⁻³%. EXTRACT 2 has no effect whatever the dose applied.

Example 3: Examples of formulations illustrating the invention and in particular the compositions according to the invention.

These compositions were obtained by simple mixing of the different constituents.

5 **Composition 1: Cream in the form of an oil-in-water emulsion**

Oily phase:

- Abil EM90 (emulsifier).....3 %
- Volatile silicone12 %
- Purcellin oil3 %
- 10 - Bentone gel 5 %
- Liquid fraction of shea butter2 %

Aqueous phase:

- Sodium salt of EDTA (sequestrating agent)0.1 %
- EXTRACT of Example 1 2 %
- 15 - Water.....qsp 100 %

The procedure for the preparation of the emulsion consists of preparing the fatty phase and of introducing it into the aqueous phase with shaking.

The cream obtained is suitable for the treatment of seborrheic dermatitis, by application to the face once or twice a day.

20 **Composition 2 : Gel**

- Glyceryl polyacrylate (Norgel).....29.5 %
- Polyacrylamide/C13-14 isoparaffins/laureth-7 (Sepigel 305).. 2 %
- Silicone oil 10 %
- Sodium salt of EDTA (sequestrating agent) 0.1 %
- 25 - EXTRACT of Example 1 2 %
- Preservative..... 0.4 %
- Water..... qsp 100 %

The procedure for the preparation of the gel consists of mixing the glyceryl polyacrylate, the Sepigel 305, the sequestrating agent and ascorbic acid in water, then of introducing the silicone oil with shaking.

The gel obtained is suitable for the treatment of a greasy skin by application to the face once or twice a day.

Composition 3: Cream in the form of a W/O emulsion

Oily phase :

	- Span 65	0.9 %
	- Glyceryl monostearate.....	3 %
10	- Hydrogenated polyisobutene	6 %
	- Volatile silicone oil	7 %
	- PEG-41 stearate (Myrj 52).....	2 %

Aqueous phase:

	- Polyacrylamide/C13-14 isoparaffins/laureth-7 (Sepigel 305)	0.9 %
15	-Sodium salt of EDTA (sequestrating agent)	0.05 %
	- Preservative.....	0.5 %
	- Glycerol.....	3 %
	- EXTRACT of Example 1	5 %
	- Water.....	qsp 100 %

20 The procedure for the preparation of the emulsion consists of dispersing the oily phase in the aqueous phase by stirring with a homogenizer.

The cream obtained is suitable for the treatment of a greasy skin by application to the face once or twice a day.

CLAIMS

1. Cosmetic composition formulated for topical administration intended to moderate the sebaceous function of the skin, characterized in that it contains an extract of decaffeinated coffee beans.
- 5 2. Composition according to Claim 1, characterized in that the extract is derived from coffee beans selected from the species *Coffea arabica* or *Coffea canephora* or *Coffea iberica*.
3. Composition according to either of the Claims 1 or 2, in which the extract is derived from roasted coffee beans.
- 10 4. Composition according to any one of the Claims 1 to 3, in which the coffee bean extract can be obtained by an aqueous-alcoholic or alcoholic extraction.
5. Composition according to Claims 1 to 4, in which the coffee bean extract represents from 0.0001% to 20% of the total weight of the composition.
- 15 6. Composition according to Claim 5, in which the coffee bean extract represents from 0.001% to 10% of the total weight of the composition.
7. Composition according to any one of the Claims 1 to 6, in which the composition is intended for the prevention and/or treatment of greasy skins.
- 20 8. Cosmetic procedure for the treatment and/or prevention of greasy skins which consists of applying to the skin, the mucous membranes and/or the keratinic fibres a composition containing a decaffeinated coffee bean extract according to one of the Claims 6 and 7.
- 25

9. Use of a decaffeinated coffee bean extract in the preparation of a composition intended to moderate the sebaceous function of the skin by topical application.
10. Use according to Claim 9, in which the extract is derived from coffee
5 beans selected from the species *Coffea arabica* or *Coffea canephora* or *Coffea iberica*.
11. Use according to either of the Claims 9 or 10, in which the extract is derived from unroasted coffee beans.
12. Use according to any one of the Claims 9 to 11, in which the coffee
10 bean extract is obtained by an aqueous-alcoholic or alcoholic extraction.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/15025

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; HUGHES, W.J. ET AL.: "Determination of organic acids and sucrose in roasted coffee by capillary gas chromatography" retrieved from STN XP002240838 abstract & JOURNAL OF FOOD SCIENCE, vol. 52, no. 4, 1987, pages 1078-1083, ---	1-7
A	EP 0 582 147 A (NESTLE SA) 9 February 1994 (1994-02-09) page 2, line 33 - line 39; table 1 --- -/--	1-7

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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